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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/848,909	05/04/2001	R. John Collier	00742/060002	7132

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EXAMINER	
PORTNER, VIRGINIA ALLEN	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 01/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/848,909	COLLIER ET AL.	
	Examiner	Art Unit	
	Ginny Portner	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10/28/2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,6,43,44,49 and 52-119* is/are pending in the application.

4a) Of the above claim(s) *43,44,49 and 65-68,70-77.79-119* is/are withdrawn from consideration.

5)☒ Claim(s) *6 and 56-64* is/are allowed.

6)☒ Claim(s) *1,52-55,68,69,77 and 78* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) *1,6,43,44,49 and 52-119* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/14/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1,6,43,44,49 and 52-119 are pending.

Claims 43,44,49 and, claims 65-68, 70-78, 80-119 are withdrawn from consideration as being drawn to a non-elected invention.

New claims 68-69, and 77-78 are also under consideration as they recite the elected species D425.

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Allowable Subject Matter

1. Claims 6, and 56-64 define over the prior art of record and are therefore allowed.

Please Note: The Office Action, paper number 05182004, examined the claims submitted and pending dated February 11,2004 and not the claims submitted and dated 05/19/2004.

Election/Restrictions

2. Newly submitted claims 65-68(in so far as claim 68 recites non-elected inventions), 70-77, 78 (in so far as claim 78 recites non-elected inventions), 80-119are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: The newly submitted claims are directed to species of invention non-elected and are structurally and functionally different from the elected invention which contains a mutation at position

D425K of the B moiety of Anthrax toxin, as directed to fusion polypeptides (a species non-elected, nor examined, and methods of use, a non-elected invention.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 65-68, 70-78, 80-119 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Response to Arguments

3. Applicant's arguments with respect to newly amended and submitted claims have been considered but are moot in view of the new ground(s) of rejection.

New Claims/New Claim Limitations/New Grounds of Rejection

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

5. Claims 1,52-55 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 52-55 recite the new phrase that defines a functional characteristic, without structural definition of the recited relative functionality through the phrase "inhibited pore-forming ability". Upon consideration of the definitions provided in the instant Specification, the examiner found the Specification define the phrase "inhibits the pore-forming ability" at page 11, lines 19-26. The phrase recited in the amended claims is not this phrase defined at page 11, but

"inhibited pore-forming ability. Upon additional consideration of definitions provided, the examiner found at page 41, support for inhibited B moieties through combining a neutralizing antibody together with a B moiety D425K mutant (see Table 5). The complex of the antibody together with the mutated B moiety is a composition the comprises a "mutated B moiety" that "has inhibited pore-forming ability relative to a naturally-occurring B moiety of an anthrax toxin. The mere recitation of a functional characteristic does not distinctly claim the invention. While the specification can be used to provide definitive support, the claims are not read in a vacuum. Rather, the claim must be definite and complete in and of itself. Limitations from the specification will not be read into the claims. The claims as they stand are incomplete and fail to provide adequate structural properties to allow for one to identify what is being claimed. The invention is not distinctly claimed.

Claim Objections

6. Claims 68 (which recites D425K) , 69, 78 (which recites D425K) and 79 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The claims depend from a withdrawn claim and therefore are unclear and not further limiting of the claim from which they depend.

1. Claims 68 (which recites D425K) , 69, 78 (which recites D425K) and 79 are rejected, as previously applied to claims 1, 52-55, and previously applied to claims 1-4,6-8,12-20,33-35,40-41,47,50-51 under 35 U.S.C. 112, first paragraph, (written description) as failing to comply with

the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The amended and new claims are directed to polypeptides that include B-moieties that comprise a portion or fragment of the an amino acid sequences set forth in the reference sequences, SEQ 21 and may evidence specific mutations and additional mutations through the recitation of "an amino acid sequence that is 95% identical to the sequence of SEQ ID NO 21".

While the B-moieties claimed are required to evidence biological activity of lacking pore-forming ability or provokes an immune response when introduced into a subject, where or what specific sites for the additional mutations, which may include insertions, additions, deletions, and substitutions for the recited changes have not been set forth in the claims. The prior art teaches (see Blaustein, RO et al, 1989) that each portion of anthrax toxin is not toxic by itself but must be combined with an additional portion in order for toxicity to be produced, therefore the recitation of the term "anthrax toxin" set forth in the claims, defines a starting material from which the B-moiety is derived.

Original descriptive support for the instantly claimed genus of B-moieties that comprise the recited mutation sites D425K, and/or deletion of any other amino acids through the recitation of the phrase "an amino acid sequence that is 95% identical to" the reference amino acid sequence does not evidence original descriptive support in the instant specification over the complete genus. No mutant B moieties for alpha hemolysin from Staphylococcus, aerolysin form Aeromonas hydrophilia, alpha toxin from Clostridium septicum, cytotoxoin from Pseudomonas

aeruginosa, hetero-oligomeric toxins (A-B5 toxins) or in the B moieties of tetanus or diphtheria toxins, as well as other oligomeric virulence factors ranging from toxins to adhesions (instant specification bridging pages 21-22) are specifically described.

While Applicant has provided written descriptive support forth clostridial and Bacillus mutant B-moieties in Table 6, and SEQ ID NO 1-18, the specification does not describe mutant B-moieties from Staphylococcus, Aeromonas, hetero-oligomeric toxin, and the genus of proteins known as toxins and oligomeric adhesions, and B-moieties that comprise any size amino acid sequence or any amino acid sequence taken from the reference sequences in any order, as the claimed products have not been described by structure correlated with function.

The instant Specification, at page 22 top of page, invites experimentation to identify additional mutant B-moieties, and dominant negative forms of other oligomeric virulence factors, ranging from toxins to adhesins. An invitation to experiment, does not show possession of the genus of B-moieties that only comprise a conserved amino acids sequence; the sequence held in common not being any consecutive number or range of amino acids from the reference sequences of the claims that would define a conserved biological function .

Possession of a screen to identify mutant B-moieties for a functional characteristic, does not show possession of show possession of a highly variable genus of B-moieties of any type of biological function, that may or may-not be detected in the screen disclosed in the instant specification. No specific distinguishing characteristics are set forth in the claims to show that the B-moieties are characteristic anthrax toxin B-moieties. The genus of moieties that correspond to anthrax toxin B-moieties are clearly within the scope of the claims, as now presented and defined in the instant Specification, but original descriptive support over the

highly variable genus that only shares "an amino acid sequence" of any size with the reference SEQ ID NO, and the additional mutational site or sites, and which do not evidence any specific biological function has not been described . Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The composition itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. Also see Office Action paper dated August 4, 2003, page 20.

Claims 68 (which recites elected invention D425K), 69, 78 (which recites D425K) and 79 do not require the polypeptide to evidence any specific size or sequence but must only comprise an amino acid sequence with 95% identical to a reference sequence of SEQ ID NO 21 and be immunogenic, but what the immune response is specific for is not recited in the claims.

Reference SEQ ID NO 21(700+ aa): ----------

Scope of what is Claimed:

Comprises 100% identity to an amino acid sequence of SEQ ID NO 21 specifically: D425K,

XXXXXXXXX - (D425K) XXXXXXXXXXXXXXXXXXXXX

Or "i.e. 5 differences for every 95 aa identical and must include (D425K)

X" different aa: XXXXX ----------

X---------X---------X---------XX----------

X---------XXXX----------

---------XXX----------XX----------

At paragraph [0013] of the instant specification, the invention is defined to include a moiety that evidences a deletion mutation of "at least 20 amino acids of the residues in the D2L2 loop of PA", a complete deletion of "all or part of the D2L2 loop and a deletion of amino acids that are N-delta or C-terminal to the loop", thus defining the claimed moiety to comprises only the required amino acid sequence of D425K and may evidence any structure together with immunogenicity that includes the D425K mutation 1 does not require the moiety to evidence any specific biological function but must only comprise an amino acid sequence with 95% identical to a reference sequence of SEQ ID NO 21

Claim Rejections - 35 USC § 112

2. Claims 68 (which recites elected invention D425K), 69, 78 (which recites D425K) and 79 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 68 (which recites D425K) , 69, 78 (which recites D425K) and 79 recite the phrase "an amino acid sequence"; the term "an" is an indefinite article, and does not set forth what the amino acid sequence that evidences the recited percent identity with SEQ ID NO 21. The claimed moiety is not required to comprise the entire amino acid sequence of SEQ Id NO 21, and includes fragments, and portions of SEQ IDNO 21 through the recitation of the term "polypeptide" , but must only comprise, for example, position 425 lysine through the positive recitation of D425K. Based upon the sequence listing provided in the instant Specification, position 425 of SEQ ID No 21 is K, therefore comprises 425K. Why is the recitation of D425K in the claims required when the sequence of SEQ ID NO 21 already comprises 425K? How

much of SEQ ID NO 21, which contains more than 735 amino acids been deleted, modified or changed? This rejection could be obviated by amending the claims to recite the phrase -------- wherein the B-moiety is 95 % identical to the amino acid sequence of SEQ ID NO 21 and position 425 is lysine --------

Conclusion

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

8. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. US Pat. 6,426,231 is cited to show pore-forming compositions..

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (571) 272-0862. The examiner can normally be reached on M-F, alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Vgp
January 19, 2005

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